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(54) PARENTERAL IRON PREPARATIONS AND PROCESS FOR THE PRODUCTION OF THE SAME

(54)

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ABSTRACT:

CLAIMS: Show all claims

*** Note: Data on abstracts and claims is shown in the official language in which it was submitted.

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Parenteral iron preparations

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Abstract

A non-ionic iron-carbohydrate complex is formed of 1 mol. of ferric hydroxide and 1 mol. of a complex-forming agent consisting of a mixture of sorbitol (about 0.4 mol.), gluconic acid (about 0.3 mol.) and a polyglucose (about 0.3 mol.), the polyglucose comprising dextrin, dextran, hydrogenated dextrin or hydrogenated dextran having intrinsic viscosity 0.01-0.025 at 25 DEG C., and average molecular weights 500-1200. The hydrogenated polyglucoses are substantially non-reducing to Somogyi reagent. The complex is made by treating 1 mol. of a trivalent iron compound in aqueous solution with about 2 mols. of complex-forming agent having the molar ratio of sorbitol: gluconic acid: polyglucose about 1.15: 0.40: 0.5, and heating the mixture at an alkalene pH. In one embodiment, aqueous solutions of ferric chloride and alkali are added to an aqueous solution of carbohydrate at 60 DEG C., and the reaction mixture (pH 9-9.5) heated to boiling for 5-30 minutes. Alternatively, a carbohydrate solution and alkali are added to an aqueous suspension of freshly-precipitated ferric hydroxide. In a further embodiment, an acid-complex is made by adding to aqueous ferric chloride, at room temperature, aqueous carbohydrate solution and sufficient sodium carbonate or bicarbonate solution to produce a pH of 2.5, increasing the pH to about 9.5 by addition of sodium hydroxide and heating to boiling. The complex is isolated by precipitation from the cooled and neutralized solution. The complex may contain 21-26% iron and aqueous solutions containing 5-10% iron may be formed therefrom for therapeutic use (Divisions A5-A6). The hydrogenation of dextrin is described.ALSO:A non-ionic iron-carbohydrate complex is formed of 1 mol of ferric hydroxide and 1 mol of a complex-forming agent consisting of a mixture of sorbitol (about 0.4 mol), gluconic acid (about 0.3 mol) and a polyglucose (about 0.3 mol), the polyglucose comprising dextrin, dextran, hydrogenated dextrin or hydrogenated dextran having intrinsic viscosity 0.01-0.025 at 25 DEG C., and average molecular weights 500-1200. The hydrogenated polyglucoses are substantially non-reducing to Somogyi reagent. The complex is made by treating 1 mol of a trivalent iron compound in aqueous solution with about 2 mols of complex-forming agent having the molar ratin of sorbitol : gluconic acid : polyglucose about 1.15:0.40:0.5, and heating the mixture at an alkaline pH. In one embodiment, aqueous solutions of ferric chloride and alkali are added to an aqueous solution of carbohydrate at 60 DEG C., and the reaction mixture (pH 9-9.5) heated to boiling for 5-30 minutes. Alternatively, a carbohydrate solution and alkali are added to an aqueous suspension of freshly-precipitated ferric hydroxide. In a further embodiment, an acid-complex is made by adding to aqueous carbohydrate solution and sufficient sodium carbonate or bicarbonate solution to produce a pH of 2.5, increasing the pH to about 9.5 by addition of sodium hydroxide and heating to boiling. The complex is isolated by precipitation from the cooled and neutralized solution. The complex may contain 21-26% iron and aqueous solutions containing 5-10% iron may be formed therefrom for therapeutic use (Division A5-A6). The hydrogenation of dextrin is described.ALSO:A therapeutic iron preparation comprises an aqueous solution of a non-ionic iron-carbohydrate complex formed of 1 mol of ferric hydroxide and 1 mol of a complex-forming agent consisting of a mixture of sorbitol (about 0.4 mol), gluconic acid (about 0.3 mol) and a poly glucose (about 0.3 mol), the poly-glucose comprising dextrin, dextran, hydrogenated dextrin or hydrogenated dextran having intrinsic viscosity 0.01-0.25 at 25 DEG C and average molecular weight 500-1200. The solution, which may contain 5-10% iron, are administered by intramuscular injection.

Parenteral iron preparations and process for the production of the same

The present invention is related to new therapeutically useful parenteral readily absorbed preparations of iron and, more in particular, preparations of iron containing a complex of trivalent iron and to a process for the production thereof.

Parenteral preparations comprising a complex of trivalent iron are already known. For instance, the saccharates of iron are produced by using sugar as a complex forming agent. These products are widely used for intravenous administration; however, they cannot be readily used for intramuscular administration because aqueous solutions thereof are highly alkaline. The iron dextrins and iron dextrans may be administered intramuscularly. However, these products have a high average molecular weight ranging generally between 100 000 and 200 000 and, therefore, are absorbed only incompletely in the human and animal body. Furthermore, the administration of these products often causes an undesired coloration at the side of injection. Trivalent iron in the form of ferric hydroxide has furthermore already been converted into complex compounds thereof by means of a mixture of gluconic acid and sorbitol. Thus, one mol of ferric hydroxide has been reacted with at least one half mol of gluconic acid and at least one half mol of sorbitol (German patent 862,482). However, these complex products do not have a sufficient stability. Recently, complex compounds of iron have been produced in a low molecular embodiment (average

particle weight about 5,000) by means of a hexitol such as sorbitol and a hydroxycarboxylic acid such as citric or gluconic acid, these products being stabilized by means of dextrins having an average molecular weight of about 1,000 to 5,000 (Canadian patent 659,420). These products are absorbed rapidly. However, about 35 % of the iron administered are excreted again within short time through the kidneys by urination (see A. Pringle et al., Lancet 1962, II, p. 749). The iron excreted in this way is lost for the curing effect in the body. Thus, in these products a rapid absorption is contrasted by a high rate of excreted, unutilized iron. Furthermore, these products have a rather high toxicity. The LD_{50} in white mice ranges to 36 mg. Fe(III)/kg. upon subcutaneous administration, 50 mg. Fe(III)/kg. upon intraperitoneal administration, and 35 mg. Fe(III/kg. upon intravenous administration (compare the first line of page 11 of Canadian patent 659,420). Possibly, the high toxicity of these products is caused by the fact that they do not have a uniform composition and contain considerable amounts of readily ionizable iron which amounts exert a toxic effect in the human body. According to Canadian patent 659,420, the hydroxycarboxylic acid and the hexitol component are bound to the iron atom while the dextrin is present in a free form and serves as a stabilizing agent for the insufficiently stable dispersion of the complex salt in water. When subjecting this product to electrophoresis, about 6 % of the iron contained in these products migrates to the anode with a higher speed than the remaining amount of iron, i.e. the product is not uniform in electrophoresis.

Therefore, it is an object of the present invention to provide a new therapeutically useful parenteral preparation of iron comprising a readily absorbed complex of trivalent iron by the use of a mixture of sorbitol, gluconic acid and certain oligosaccharides as complex forming agent which complex of trivalent

iron is non-ionic, has a uniform composition and a low toxicity and at the same time has a high rate of utilization of the iron administered to the human or animal body.

Further objects of the present invention and advantages thereof will become apparent as the description proceeds.

The new therapeutically useful preparations of iron according to the present invention comprise a non-ionic (electrophoretically uniform) complex of trivalent iron as ferric hydroxide with a complex forming agent consisting of sorbitol, gluconic acid and certain oligosaccharides (polyglucoses) in very particular proportions and amounts. The complex forming agent consists of sorbitol, gluconic acid and, as third component, a dextrin or dextran having an average intrinsic viscosity of about 0,01 to about 0,025 at 25°C. and an average molecular weight of from about 500 to about 1200 or a hydrogenated dextrin or dextran having said average intrinsic viscosity and said average molecular weight and being substantially non-reducing to the Somogyi reagent, or mixtures thereof, in a molar ratio of about 0,4 mol of sorbitol : about 0,3 mol of gluconic acid : 0,3 mole of the above polyglucose. About 1 mol of said complex forming agent is present in the iron preparation according to the present invention per each mol of trivalent iron or ferric hydroxide.

The dextrans and dextrins of such an average molecular weight are obtained by known methods, such as by growing under carefully controlled conditions of temperature, appropriate organism in a suitable nutrient medium containing a high proportion of sucrose or by controlled acid hydrolysis of native dextrans and dextrins or they may be obtained synthetically, as described for instance in US Patent 3,022,221 and Römpp Chemielexikon, 4th edition, 1958, column 1021-1022.

The hydrogenated dextrans and dextrins may be produced according to known methods, such as by subjecting a dextran or dextrin

of the average molecular weight defined hereinabove to reaction with sodium boro-hydride in an aqueous medium or by catalytic hydrogenation as described for instance in US Patents 2,807,610 or 3,022,221 or in J.Am.Chem.Soc. 74 (1952), pgs. 2126-2127.

The Somogyi reagent is defined for instance in J.Biol.Chem. 70, 607 (1926).

The iron preparations according to the present invention are prepared by subjecting 1 mol of a compound of trivalent iron in a reactive form to reaction with about 2 mols of the complex forming agent above defined, however containing its ingredients in a molar ratio of about 1,15 mols of sorbitol : about 0,4 mol of gluconic acid : about 0,5 mol of the above polyglucose, in an aqueous medium and heating the resulting mixture after an alkali is added thereto until a pH of about 9,5 or somewhat above is reached. Complex formation may take place both at an alkaline pH and at an acid pH with the intermediate formation of an acid complex. Preferably, an alkali metal hydroxide, preferably sodium hydroxide is used as alkali.

The word "about", as herein used, is to be understood in such a way that changes ranging to about ± 20 % in the ratio of the components of the complex forming agent among each other and in the ratio between the ferric hydroxide and the complex forming agent are allowable. The process according to the invention with the other respects should be carried out for fulfilling the objects of the invention in such a way that electrophoretically uniform, low molecular complexes are obtained wherein all of the three complex forming agents are bound in a complex form.

The trivalent iron compounds used as starting materials in the process according to the present invention correspond to the trivalent iron compounds which have been used already in similar known processes. Preferably, ferric chloride is used as starting material which in the alkaline complex formation is converted

into trivalent iron hydroxide (ferric hydroxide) by reaction with soda, sodium bicarbonate or aqueous sodium hydroxide and is further reacted with the complex forming agent in a freshly precipitated reactive form, preferably after being washed. The formation of the iron hydroxide is carried out according to known methods in such a way that its reactive polynuclear γ-form is formed to an extent as large as possible and the formation of its less reactive polynuclear α-form is avoided. In the alkaline complex formation, the alkali such as the aqueous sodium hydroxide is added to the solution of the iron compound in such an amount that the acid yielding from the iron compound is neutralized and (after complete neutralization) an excess of about 0,25 mols of NaOH per 1 gram atom Fe remains in the reaction mixture. The pH-value of the reaction mixture should be at about 9 - 9,5 during the alkaline complex formation. During the reaction a small amount of alkali is consumed. After the termination of the reaction it should be possible to determine 0,25 mols of NaOH by titration. When using $FeCl_3$ as starting material, preferably 3,5 mols of NaOH are used per one mol of $FeCl_3$. In the alkaline complex formation, preferably the solution of the complex forming agents in water is placed in the reaction vessel and is heated at 60°C. the solution of the iron compound, for instance, the ferric chloride, as well as the aqueous sodium hydroxide is introduced into the reaction mixture as separate solutions (one solution of ferric chloride and the other solution of sodium hydroxide) in the calculated amount. Thus, the complex, i.e. a clear solution is produced very rapidly. Only during the final stage of the addition of both solutions small amounts or precipitates may occur which are dissolved again during the following heating. After the addition of the solutions is terminated, the reaction mixture is heated to boiling for a period of about 5 to 30 minutes, preferably for about 30 minutes, thus producing a clear solution and an increased degree

of stabilization.

However, the formation of the complex of trivalent iron in an alkaline medium may be also carried out by placing a suspension of freshly precipitated and washed ferric hydroxide into the reaction vessel, adding the complex forming agents and the alkali necessary for controlling the pH-value thereto, and heating to boiling the thus obtained reaction mixture until a clear solution is obtained.

The new complex preparation of iron according to the present invention may be furthermore produced by preparing in a first step and "acid complex" and converting the same into the desired complex of trivalent iron by heating the "acid complex" in an aqueous alkaline medium. The "acid complex" may for instance be prepared by adding such an amount of an aqueous solution of sodium carbonate or sodium bicarbonate to an aqueous solution of ferric chloride and 2 mols of the above defined complex forming agent per each mol of ferric chloride slowly at room temperature that the pH-value of the reaction solution rises to about 2,5. The color of the reaction mixture thereby is converted to a reddish brown. The formation of the acid complex is proven by the addition of methanol to a sample of the thus obtained solution, thus producing a precipitate containing both iron and the complex forming agent; in contrast thereto, a solution of ferric chloride which does not contain the complex forming agent or a solution of the complex forming agent which does not contain ferric chloride does not produce a precipitate at equivalent conditions, i.e. the salt of iron or, respectively, the components of the complex forming agent in these essays remain in solution. They stay in solution even if a very large amount of methyl alcohol is added.

When now increasing the pH-value of the solution of the acid complex obtained in the first step from 2,5 to about 9,5, which for instance may be effected by adding corresponding amounts of

aqueous sodium hydroxide, a precipitate is formed from a pH of about 3 which precipitate however redissolves almost completely during the further addition of the alkali metal hydroxide until pH 9,5. This addition of sodium hydroxide from pH 2,5 is carried out at room temperature. After the pH of about 9,5 is reached, the reaction mixture is heated to boiling for a short period, immediately cooled again, brought to a pH-value of about 7,0 by the addition of a physiologically harmless acid such as preferably hydrochloric acid and is worked up.

The ratio between water and solid materials in the alkaline and in the acid procedure should be preferably controlled in such a way that 2 to 4 parts by weight of water are present per each part by weight of solid material.

The final products obtainable by the process according to the present invention have the following properties:

The gluconic acid contained in the complex forming agent mixture used in accordance with the present invention produces a good stability of the complex thus obtained to heat both at the neutral pH and in a weakly acid pH range. This indicates that the content of gluconic acid produces a favorable effect to thermostability in view of the change of the isoelectric point. By too high a content of gluconic acid, the stability of the complex would in contrast thereto be decreased which would result in a higher toxicity of the complex salt. The sorbitol and in particular the oligosaccharide (polyglucose) favorably influence the formation of a uniform complex and thus decrease the toxicity and, respectively, increase the compatibility of the iron preparation according to the present invention in a very favorable manner. By using low molecular oligosaccharides having an average molecular weight of only about 500 to about 1200, it is on the other hand avoided that the average particle size of the ferric complex formed is to high-molecular and the absorption of the complex is descreased to too

large an extent.

Subjecting the product of the invention to electrophoresis shows that the iron complex compounds according to the invention migrate as a uniform complex to the anode at pH 7,4 and 8,6 and therefore are negatively charged. The complex preparations may be precipitated from their aqueous solutions in manners known per se by the addition of organic solvents miscible with water. The iron content of the dried preparations is about 21 to 26 %. Without any difficulty aqueous solutions containing from 5 to 10 % of iron may be prepared from said dry preparations. These aqueous solutions are stable on sterilization thereof in a current of steam.

When tested pharmacologically and in the clinics the preparations prepared in accordance with the present invention showed to be well tolerated and highly effective in the treatment of iron deficiencies.

The means lethal dose upon intramuscular injection of a solution of the complex containing 5 to 10 % of trivalent iron to mice was about 350 mg. of Fe/kg. in a 10-days-test.

The means lethal dose upon intramuscular injection of a solution of the complex containing 5 % of trivalent iron to guinea-pigs in a 10-days-test was above 350 mg. of trivalent Fe per kg. Multiple intramuscular injections during 101 days with a total dose of 450 mg. of trivalent iron per kg. were well tolerated and did not affect the normal growth of the guinea-pigs.

With rats suffering from lead poisoning anemia, the erythrocyte number increased upon intramuscular administration of the complex in a dose of 10 mg. of trivalent iron per kg. in comparison to check test animals. When administering a single intramuscular dose of 2 ml. of the solution of the complex corresponding to 100 mg. of trivalent iron to suckling pigs on the 4th day after birth, an increase of the erythrocyte number from 4,6 to 6,9 Mio/cb.mm. and of the hemoglobine content from 10,4 to 11,9 g. per

100 ml. was observed on the 53rd day after birth.

In the clinical test the preparations according to the present invention showed to be effective and well tolerated. Upon intramuscular injection of the complex, the patients excreted by urination on an average only 10 % of the iron amount administered.

No coloration at the side of injection appeared upon intramuscular injection of the preparations prepared in accordance with the present invention.

The absorption of the preparations was very good. The preparations were very quickly carried away from the side of intramuscular injection. Thus, for instance in rabbits, only 2,9 % of the iron was determined as residue in the place of injection after 4 days since intramuscular injection of 10 mg. of iron as complex per kg. of animal body. In piglets, the injected iron has disappeared at the side of administration within few days after the injection of the complex.

It follows from the above given properties that the preparations prepared in accordance with the present invention produce a considerable advance in the art in comparison to known iron preparations.

In contrast to the products produced in accordance with Canadian patent 659,420, the products according to the present invention are non-ionic, electrophoretically uniform complex compounds containing all of the three components of the complex forming agent bound in a complex form thus avoiding the formation of components containing ionizable iron. The toxicity of the products produced in accordance with the present application is considerably lower than that of the products according to said Canadian patent 659,420. Furthermore, the amount of iron which is not used in the human body, i.e. which is excreted by urination through the kidneys is much lower with the products according to the present application than with the products according

to the Canadian patent. This is achieved by the particular ratios between the amounts of the components of the complex forming agent and of the iron and by the particular process conditions of the present invention.

The following examples serve to further illustrate the present invention without however limiting the same thereto:

Example 1

45 g. of sodium borohydride dissolved in water are added to a 10 % w/v aqueous solution containing 1 kg of a dextrin having an average molecular weight of about 1000 and an average intrinsic viscosity of 0,02.

The mixture is allowed to stand at room temperature for 5 hours with occasional stirring, and then is acidified with 30 % acetic acid. The acidified mixture is passed successively through a column of a cation exchange resin and an anion exchange resin. Methyl alcohol is added to the thus deionized solution with stirring to give a solution containing 80 % of methyl alcohol by volume. After standing for 24 hours at 25°C., the supernatant solution is decanted from the precipitated hydrogenated dextrin. The product is dried at 100°C. at atmospheric pressure for one hour, then at 100°C. in vacuum for two hours. The product is non-reducing to the Somogyi reagent. It has an average intrinsic viscosity of 0,02 at 25°C.

Example 2

284 g. of sorbitol, 81 g. of sodium gluconate and 108 g. of the hydrogenated dextrin having an average molecular weight of about 1000 and an average intrinsic viscosity of about 0.02, obtained as described in Example 1, are added to a suspension of ferric hydroxide containing 56 g. Fe and being freshly prepared by reacting 920 g. of an aqueous 30 g./g.% ferric chloride ($FeCl_3.6H_2O$) solution with a solution and washing until free from electrolytes) in 200 ml. of water with rapid stirring. The pH

of the reaction mixture is brought to a value of 12 by the addition of 50 ml. of 10 N aqueous sodium hydroxide and is then heated to 80°C. Thereby, the iron hydroxide dissolves starting from 50°C., and at 80°C. a complete solution is obtained which is heated to boiling for 15 minutes. The pH of the cooled solution is brought to a value of 7.0 by the addition of hydrochloric acid and the iron complex is isolated therefrom by precipitation with methanol in a ratio of one part of the solution per 1,5 parts of 99 % methanol. The precipitate is filtered off and the complex is dried. The iron content of the dried preparation amounts to 25,7 %. An aqueous solution containing 5 % of iron is prepared from this dry preparation which solution is filled into ampoules and is sterilized by heating the ampoules for 30 minutes in a current of steam.

Example 3

42 g. of sorbitol, 12 g. of sodium gluconate, and 16 g. of a hydrogenated oligomeric dextrin having an average molecular weight of about 1000 and an average intrinsic viscosity of 0,02 are dissolved in such an amount of water to yield a solution of 250 g. The solution is heated to 60°C. 95 g. of 10 N aqueous sodium hydroxide and 184 g. of a 30 weight by weight % aqueous solution of ferric chloride $FeCl_3$ (d = 1,162 are added simultaneously with rapid stirring in such a way that the reaction mixture always has a pH between 9,0 to 9,5. When proceeding in this way the ferric hydroxide is immediately dissolved. After the addition of the reaction components is terminated, the reaction mixture is heated to boiling for 20 minutes and then is cooled. Hydrochloric acid is added until a pH of 7,0 is reached, the solution is filtered and the iron hydroxide complex is isolated by precipitation with acetone in a ratio of one part of the solution per 1,5 parts of acetone and the isolated complex is dried. Iron content: 22,8 % by weight of Fe. This dry preparation is dissolved in water to yield a solution containing 10 % of iron, the solution is filled

into ampoules and the ampoules are sterilized for 30 minutes in a current of steam.

Example 4

A mixture of 42 g. of sorbitol, 12 g. of sodium gluconate, 16 g. of a hydrogenated oligomeric dextrin having an average molecular weight of about 800 and an average intrinsic viscosity of 0,015 and 30 g. of water is added to 184 g. of a 30 weight by weight % aqueous solution of ferric chloride $FeCl_3$ (d = 1,162) at room temperature and 140 ml. of a 20 weight per volume % solution of soda is slowly added thereto with rapid stirring. The pH-value of the reaction mixture rises during the addition from 0,6 to 2,5 and the color thereof changes to reddish brown. Thereafter, 20,5 ml. of a 10 N aqueous sodium hydroxide solution are added, thus causing the pH to rise to 9,5. Starting from a pH-value of 3, a ferric oxychloride complex is precipitated which almost completely is redissolved at room temperature during the further addition of the alkali hydroxide until a pH-value of 9,5 is reached. Thereafter, the reaction mixture is heated to boiling, immediately thereafter cooled to room temperature and neutralized to a pH of 7,0 by the addition of hydrochloric acid and is worked up as described in Example 3. The iron content of the resulting preparation is 26,0%.

Example 5

When proceeding as described in Example 2 and using 108 g. of a dextrin having an average molecular weight of about 1000 and and average intrinsic viscosity of about 0,02 in place of the hydrogenated dextrin product, a dry preparation is obtained which contains 23,6 % of trivalent iron. It is dissolved in water, filled into ampoules and is sterilized as described in Example 2. The dextrin-fraction with an average intrinsic viscosity of about 0,02 is obtained by acid hydrolization and precipitation of the neutralized solution with methanol of a dextrin having an

average intrinsic viscosity of about 0,055 (see US patent 3,076, 798) derived from potato starch.

Example 6

42 g. of sorbitol, 12 g. of gluconic acid, and 16 g. of a dextran having an average molecular weight of about 1000 and an average intrinsic viscosity of about 0,02 are reacted with ferric hydroxide prepared in situ as described in Example 2. This dextran is obtained by acid hydrolization and precipitation of the neutralized solution with methanol, of a dextran having an average intrinsic viscosity greater than 0,1 at 25°C. (see US Patent 3,100,202).

Example 7

A hydrogenated dextran having an average molecular weight of about 1000 and an average intrinsic viscosity of about 0,02 is used as described in Example 6 in place of the dextran, in order to prepare a dry preparation containing 22,8 % by weight of Fe. The hydrogenated dextran is obtained from a dextran as described in Example 6 by hydrogenation according to Example 1. The resulting product is non-reducing to the Somogyi reagent.

According to Example 2 a product is obtained, the iron content of which amounts to 25,7 %. This corresponds to an $(FeOOH)_n$ content of 40,8 % (MW 89). The residual 59,2 % are the complex forming compounds in relation 0,4 mol sorbitol : 0,3 mol gluconic acid : 0,3 mol polyglucose. This molar relationship corresponds to the following weight relationship: 23,7 % sorbitol : 19,2 % gluconic acid : 16,3 % polyglucose.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. The process of preparing a therapeutically useful preparation of iron comprising a non-ionic ferric complex which comprises subjecting 1 mol of iron-(III) hydroxide in a reactive form selected from the group consisting of freshly prepared iron-(III)-hydroxide and iron-(III) hydroxide prepared in situ to reaction with about 2 mols of a complex forming agent consisting of sorbitol, gluconic acid and a polyglucose selected from the group consisting of the dextrins and dextrans having an average intrinsic viscosity of about 0,01 to about 0,025 at 25°C. and an average molecular weight of from about 500 to about 1200 and of the hydrogenated dextrins and dextrans having an average intrinsic viscosity of about 0,01 to about 0,025 at 25°C. and an average molecular weight of from about 500 to about 1200 and being substantially non-reducing to the Somogyi reagent, in a molar ratio of about 1,15 mols of sorbitol per about 0,40 mol of gluconic acid per 0,5 mol of polyglucose.

2. The process according to claim 1 which comprises heating 1 mol of freshly precipitated ferric hydroxide in a reactive form together with about 2 mols of the complex forming agent in an aqueous alkaline medium until the ferric hydroxide is dissolved.

3. The process according to claim 1 which comprises adding 2 mols of the complex forming agent to an acid aqueous solution of 1 mol of a ferric salt, adding slowly at about room temperature an alkali to the thus obtained acid solution until a pH of about 2,5 is reached, thereafter further adding an alkali thereto until a pH of 9,5 is reached, and heating the thus obtained alkaline solution to boiling for about 5 to about 30 minutes.

4. A therapeutically useful preparation of iron comprising a non-ionic ferric complex whenever prepared by the process of claim 1, 2 or 3 or an obvious chemical equivalent thereof.

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